

What is claimed:

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1. An isolated nucleic acid molecule which encodes an AGS protein, comprising a nucleotide sequence having at least 86% identity to the nucleotide sequence of SEQ ID NO:1, or the complement thereof.

2. The isolated nucleic acid molecule of claim 1, which comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or the complement of SEQ ID NO: 1 or SEQ ID NO: 3.

10 3. The isolated nucleic acid molecule of claim 1, which comprises a nucleotide sequence having at least 95% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3, or the complement of SEQ ID NO: 1 or SEQ ID NO: 3.

15 4. The isolated nucleic acid molecule of claim 1, which comprises the nucleotide sequence of SEQ ID NO:1, or the complement thereof.

5. The isolated nucleic acid molecule of claim 1, which comprises the nucleotide sequence of SEQ ID NO: 3, or the complement thereof.

20 6. The isolated nucleic acid molecule of claim 1, which encodes a protein that activates G protein-coupled signal transduction in a G protein-coupled receptor independent manner. *B*

25 7. The isolated nucleic acid molecule of claim 1, which is a human nucleic acid molecule.

8. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a protein which comprises an amino acid sequence having at least 97% identity to the amino acid sequence of SEQ ID NO:2.

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9. The isolated nucleic acid molecule of claim 8, wherein the protein comprises an amino acid sequence having at least 98% identity to the amino acid sequence of SEQ ID NO:2.

5 10. The isolated nucleic acid molecule of claim 8, wherein the protein comprises an amino acid sequence having at least 99% identity to the amino acid sequence of SEQ ID NO:2.

10 11. The isolated nucleic acid molecule of claim 8, which encodes a protein comprising the amino acid sequence of SEQ ID NO:2.

15 12. The isolated nucleic acid molecule of claim 8, wherein said protein activates G protein-coupled signal transduction in a G protein-coupled receptor independent manner.

15 13. The isolated nucleic acid molecule of claim 8, which is a human nucleic acid molecule.

20 14. A vector comprising the nucleic acid molecule of claim 1.

20 15. The vector of claim 14, which is a recombinant expression vector.

25 16. A host cell containing the vector of claim 14.

25 17. A method for producing an AGS protein comprising culturing the host cell of claim 16 in a suitable medium such that AGS protein is produced.

30 18. The method of claim 17, further comprising isolating an AGS protein from the medium or the host cell.

19. A nonhuman transgenic animal which contains cells carrying a transgene encoding an AGS protein.

20. An isolated AGS protein comprising an amino acid sequence having at least 97% identity to the amino acid sequence of SEQ ID NO:2.

5 21. The isolated protein of claim 20, comprising an amino acid sequence having at least 98% identity to the amino acid sequence of SEQ ID NO:2.

10 22. The isolated protein of claim 20, comprising an amino acid sequence having at least 99% identity to the amino acid sequence of SEQ ID NO:2.

15 23. The isolated protein of claim 20, comprising the amino acid sequence of SEQ ID NO:2.

20 24. A fusion protein comprising at least a portion of the AGS protein of claim 20, operatively linked to a non-AGS polypeptide.

25 25. An antibody that specifically binds the AGS protein of claim 20.

26. The antibody of claim 25, which is monoclonal.

27. The antibody of claim 25, which is labeled with a detectable substance.

28. A pharmaceutical composition comprising the protein of claim 20 and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition comprising the antibody of claim 25 and a pharmaceutically acceptable carrier.

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30. A method for identifying a compound that modulates signal transduction in a cell, comprising:

contacting a cell that expresses an AGS protein with a test compound;

determining the effect of the test compound on the activity of the AGS protein;

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identifying the test compound as a modulator of signal transduction based on the ability of the compound to modulate the activity of the AGS protein in the cell.

31. The method of claim 30, wherein the AGS protein comprises an amino acid sequence having at least 97% identity to SEQ ID NO: 2 and stimulates G protein activity in a receptor-independent manner.

32. The method of claim 30, wherein the AGS protein is human.

15 33. The method of claim 30, wherein the AGS protein comprises the amino acid sequence of SEQ ID NO: 2.

34. The method of claim 30, wherein the cell has been engineered to express the AGS protein by introducing into the cell an expression vector encoding the AGS 20 protein.

35. The method of claim 30, wherein the cell has further been engineered to express a G protein α subunit.

25 36. The method of claim 30, wherein the cell is a yeast cell that has been engineered to express a mammalian or chimeric G protein α subunit and the effect of the test compound on the activity of the AGS protein is determined by monitoring a pheromone response pathway in the yeast cells.

37. The method of claim 36, wherein the yeast cell has been engineered to express a G_pα1-G_αi2 chimeric G protein α subunit.

38. The method of claim 36, wherein the pheromone response pathway in the yeast cells is monitored by measuring the activity of a pheromone responsive promoter in the yeast cells.

39. The method of claim 30, wherein the effect of the test compound on the activity of the AGS protein is determined by monitoring the ability of the test compound to bind to the AGS protein.

40. The method of claim 30, wherein the effect of the test compound on the activity of the AGS protein is determined by monitoring the ability of the test compound to modulate the interaction of the AGS protein with a target molecule.

41. The method of claim 40, wherein the target molecule is a G protein.

42. A method for modulating G protein coupled signal transduction in a cell comprising contacting a cell with an agent which modulates AGS protein activity or AGS nucleic acid expression such that G protein coupled signal transduction is modulated in the cell, when compared with G protein coupled signal transduction in the cell in the absence of the agent.

43. The method of claim 42, wherein the cell-associated activity is a G-protein mediated activity.

44. The method of claim 42, wherein the agent stimulates an AGS protein activity or AGS gene expression.

45. The method of claim 42, wherein the agent is an active AGS protein.

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46. The method of claim 42, wherein the agent is a nucleic acid encoding an AGS that has been introduced into the cell.

47. The method of claim 42, wherein the agent inhibits an AGS protein 5 activity or AGS gene expression.

48. The method of claim 42, wherein the agent is an antisense AGS nucleic acid molecule.

10 49. The method of claim 42, wherein the agent is an antibody that specifically binds to an AGS protein.

50. The method of claim 42, ~~wherein~~ the cell is present within a subject and the agent is administered to the subject.

15 51. A method for treating a subject having a disorder characterized by an aberrant AGS protein activity or nucleic acid expression comprising administering to the subject an AGS modulator such that treatment of the subject occurs.

20 52. A method for detecting the presence of an AGS protein in a biological sample comprising contacting a biological sample with an agent capable of detecting the AGS protein or mRNA such that the presence of the AGS protein is detected in the biological sample.

25 53. The method of claim 52, wherein the agent is a labeled or labelable nucleic acid probe capable of hybridizing to an AGS mRNA.

54. The method of claim 52, wherein the agent is a labeled or labelable antibody capable of specifically binding to an AGS protein.

55. A method for identifying a compound that activates a signal transduction pathway in a cell, said method comprising,
providing a cell that undergoes a measurable change when the signal transduction pathway is activated;
5 contacting the cell with a test compound; and
determining if the test compound causes a measurable change to thereby identify the test compound as a modulator of the signal transduction pathway.

10 56. The method of claim 55, wherein said signal transduction pathway is a G protein signaling pathway.

15 57. The method of claim 56, wherein said cell is a yeast cell.

15 58. The method of claim 57, wherein said G protein signaling pathway is the yeast pheromone response pathway.

59. The method of claim 58, wherein said compound is a polypeptide encoded by a nucleic acid molecule.

20 60. The method of claim 59, wherein said nucleic acid comprises a nucleotide sequence having at least 70% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

25 61. The method of claim 59, wherein said nucleic acid comprises a nucleotide sequence having at least 80% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

30 62. The method of claim 59, wherein said nucleic acid comprises a nucleotide sequence having at least 90% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

63. The method of claim 59, wherein said nucleic acid comprises a nucleotide sequence having at least 95% identity to the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3.

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64. The method of claim 59, wherein said nucleic acid comprises the nucleotide sequence of SEQ ID NO:1.

65. The method of claim 59, wherein said nucleic acid comprises the 10 nucleotide sequence of SEQ ID NO: 3.

66. The method of claim 59, wherein said polypeptide activates G protein signaling in a G protein coupled-receptor independent manner.

15 67. The method of claim 59, wherein said nucleic acid comprises a nucleotide sequence which is a human.

68. The method of claim 59, wherein said polypeptide comprises an amino acid sequence having at least 97% identity to the amino acid sequence of SEQ ID NO:2.

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69. The method of claim 59, wherein the polypeptide comprises an amino acid sequence having at least 98% identity to the amino acid sequence of SEQ ID NO:2.

70. The method of claim 59, wherein the polypeptide comprises an amino 25 acid sequence having at least 99% identity to the amino acid sequence of SEQ ID NO:2.

71. The method of claim 59, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:2.

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72. The method of claim 30, wherein the compound is a nucleic acid encoding a polypeptide capable of inhibiting the activity of the AGS protein.

73. The method of claim 72, wherein said nucleic acid comprises the sequence provided in SEQ ID NO: 24.

5 74. The method of claim 72, wherein said nucleic acid encodes the polypeptide sequence provided in SEQ ID NO: 25.

75. The method of claim 30, wherein the cell further comprises a nucleic acid encoding an inhibitor of the AGS protein.

10 76. The method of claim 75, wherein said nucleic acid comprises the sequence provided in SEQ ID NO: 24.

15 77. The method of claim 75, wherein said nucleic acid encodes the polypeptide sequence provided in SEQ ID NO: 25.

78. The method of claim 75, wherein said ability of the test compound to modulate the activity of the AGS protein indicates that the test compound is a modulator of the inhibitor of the AGS protein.

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